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DOI:

[10.1016/j.cortex.2017.08.012](https://doi.org/10.1016/j.cortex.2017.08.012)

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Document Version

Peer reviewed version

Citation for published version (Harvard):

Westwood, SJ, Olson, A, Miall, C & Romani, C 2017, 'tDCS modulation of naming in healthy participants: Negative results and still no explanation – A response to a commentary by Gauvin et al. (2017)', *Cortex*.
<https://doi.org/10.1016/j.cortex.2017.08.012>

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Accepted Manuscript

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PII: S0010-9452(17)30267-8

DOI: [10.1016/j.cortex.2017.08.012](https://doi.org/10.1016/j.cortex.2017.08.012)

Reference: CORTEX 2095

To appear in: *Cortex*

Received Date: 24 July 2017

Revised Date: 0010-9452 October 0010-9452

Accepted Date: 7 August 2017

Please cite this article as: Westwood SJ, Olson A, Miall RC, Romani C, tDCS modulation of naming in healthy participants: Negative results and still no explanation – a response to a commentary by Gauvin et al. (2017), *CORTEX* (2017), doi: 10.1016/j.cortex.2017.08.012.

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tDCS modulation of naming in healthy participants: Negative results and still no explanation – a response to a commentary by Gauvin et al. (2017).

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1. Introduction

We would like to thank Drs. Gauvin, Meinzer and de Zubicaray for their commentary on our paper, Westwood, Olson, Miall, Nappo and Romani (2017). Commentaries are essential to scientific debate because they point out limits to research that may otherwise go unnoticed by the reader. This is especially needed in the field of tDCS, where there is debate regarding its efficacy. Our paper was motivated as an original contribution to this debate, so we gladly accept our chance to respond to the commentary, hereafter referred to as Gauvin et al. We first clarify two issues that frame much of what is discussed later.

Firstly, the focus of our investigation was much wider than Gauvin et al. suggested. We wanted to assess whether a single session of anodal tDCS can modify performance on *word production* tasks in healthy participants, as we made clear throughout, including in the abstract, introduction and above all in the detailed empirical investigation. In our main analyses, we looked at the general effects of anodal tDCS on word reading and picture naming speed and accuracy. Since we failed to find any significant effects in the main analyses, we attempted to find effects with a number of additional analyses of semantic interference effects, of responses at different speeds and by considering possible individual differences in response to tDCS. This amounted to roughly 80 analyses overall, none of which showed significant effects of tDCS. That Gauvin et al. focused on our analyses of semantic interference effects alone misrepresents its aims.

Secondly, and more importantly, the focus of our paper was *not* to replicate any specific study. As we explained in the introduction, one aim was to ‘try to replicate...findings’ that anodal tDCS can modify semantic interference effects, given the inconsistency of these findings. We wanted to give the effects of tDCS the best chance to emerge through different analyses, not to replicate a specific study. There is a difference between a *conceptual* replication and a *direct* replication (for discussion, see Cesario, 2014; Schmidt, 2009; Simons, 2014; Stroebe & Strack, 2014). Gauvin et al. failed to appreciate this distinction.

2. Our Response to Comments

Gauvin et al. criticized the investigations reported in our paper in terms of the theoretical framework, design, methodology and data analysis. We consider their objections in turn.

2.1. Issues with Theoretical Framework

Gauvin et al. said that a key assumption of our study was that the left inferior frontal gyrus (or LIFG) is reliably involved in semantic interference effects. This is not true. In line with the focus of the paper, our key assumption was that the LIFG underpins word production, which is line with data collected over many years from several lines of research (see Devlin, & Watkins, 2007; Indefrey & Levelt, 2004; Lazhr & Mohr, 2011; Price, 2000). Exploring the possible modulation of semantic interference effects in picture naming with LIFG stimulation was therefore a necessary aspect of our investigation. In addition, the LIFG has been the focus of a number of previous studies exploring the effects of tDCS on semantic interference, albeit with inconsistent results, as cited in our paper (e.g., Meinzer, Yetim, McMahon, & de Zubicaray, 2016; Pisoni, Papagno, & Cattaneo, 2012; Wirth et al., 2011). Far from being unaware of the current debate regarding the role the LIFG plays in semantic interference, as claimed by Gauvin et al., our hypotheses are clearly formulated in light of this debate. We state that the hypothesis that interference effects will be reduced with LIFG stimulation depends on the controversial assumption that “top-down frontal mechanisms contribute to lexical selection in addition to mechanisms of lateral inhibition intrinsic to the lexical module (see Hamilton & Martin, 2005, 2007 for a discussion)’. See page 66.

2.2. Issues with Stimulation Protocol

Gauvin et al. said that the ‘sole experiment involving an attempted replication of prior work’ was our Experiment 2, since three previous similar studies had coupled prefrontal tDCS with the cyclic blocked naming task. They then go on to say that while ‘...Westwood et al. discuss their findings from Experiment 2 in terms of a failure to replicate prior work, it is clear from Table 1 that their tDCS protocol matches none of the previous studies’.

Firstly, as already mentioned, we never set out to directly replicate a specific protocol, but instead we used parameters considered ‘best practice’. Thus, our study shared important aspects with other studies without exactly replicating any of them. Across these studies (including ours), all targeted the LIFG (except for: Wirth et al. (2011), which targeted the left dorsolateral prefrontal cortex); all used online stimulation (except for: Pisoni et al. 2012, which used offline stimulation), and all used the same location and size of the reference electrode (except for: Meinzer et al., 2016, which used 100cm² sized reference). One

departure of note is that we used a smaller active electrode compared to others (25 versus 35cm²), which was motivated by evidence that reducing the size of the active electrode can increase focality (Nitsche et al., 2008), and that this electrode size has been used with success elsewhere (see review by Mancuso, Ilieva, Hamilton, & Farah (2016). Moreover, because the efficacy of stimulation relies partly on current density (i.e., the current intensity relative to the electrode size), our use of 1.5mA current meant the current density we applied fell within the range used by the three other studies reported in Table 1 (mA/cm² of .03, .04, .06; ours, .06). Thus, we consider a difference in electrode size to be a minor departure from previous protocols, which – if anything – should have increased the likelihood of a significant effect.

Secondly, Gauvin et al. considered the use of online stimulation as an important limitation to our study. Meinzer et al. (2016) interpreted their weak effect of LIFG stimulation as potentially due to the use of online stimulation, and suggested that differences in online/offline stimulation could explain variability in the effects reported with tDCS coupled with blocked cyclic naming. We, like Meinzer et al. (2016), chose online stimulation because it is thought to target neuronal networks recruited by the task (for a similar argument, see Miniussi, Harris, & Ruzzoli, 2013), because it is considered to produce a stronger increase in excitability compared to offline stimulation (Stagg et al. 2013; Rae et al. 2013; see also, Martin et al., 2013) and because positive effects were reported by previous picture naming studies (e.g., Ross, McCoy, Wolk, Coslett, & Olson, 2010; Fertonani, Brambilla, Cotelli & Miniussi, 2014), including studies listed in Table 1.

Finally, it is certainly true that departures in protocol may result in variation in outcome, as pointed out by Gauvin et al. The problem is that we have not yet identified the conditions in which tDCS can operate reliably, at least within the limit set by our studies (i.e., word production, healthy participants, one stimulation session). Direct replications are a good way to evaluate the reliability/efficacy of protocols, which is why our lab is currently conducting several replications of studies, including Meinzer et al. (2016) and Pisoni et al. (2012). We are continuing in our efforts to establish the conditions under which tDCS is effective.

2.3. Issues with Design and Methodology

Gauvin et al. criticized two main aspects of our methodology, namely the task instructions and the use of both naming and reading tasks.

2.3.1. *Longer Reaction Times*

Gauvin et al. noticed that our picture naming reaction times (RTs) are longer than in other studies using the continuous picture naming task that they cite (e.g., Howard, Nickels, Coltheart, & Cole-Virtue, 2006, 610 to 735ms; Navarrete, Mahon, & Caramazza, 2010; 770 to 844 ms; Belke, 750 to 830ms; our 900-990ms). They attribute this to our instruction to ask participants to use subordinate names, which, according to them, deviates from previous studies using the continuous picture naming task (e.g., Howard, Nickels, Coltheart, & Cole-Virtue, 2006), and may have resulted in a processing cost, as evidence by the fact that our RTs are roughly 150ms longer than previous studies they cite.

Firstly, we did not use the term ‘subordinate names’ in task instructions, but we did ask participants to use precise names, and provided a clear example of what we mean – e.g., correct responses to water-lily could be “water-lily” or “lily” but not “flower” – along with a practice task. These instructions were to prevent participants from applying the same general term to all members of a given category, such as *flower*, which would have reduced (or abolished) the interference effect. This instruction does not contrast at all with Howard et al. (2006), who designed the original continuous naming task. In fact, it is required by this task. For example, Howard et al. (2006) included pictures of a *cap*, *beret*, *swordfish*, *wasp*, *ladybird*, and *desk*. As with our study, it was important that participants used specific words rather than more generic terms such as *hat*, *fish*, *insect*, or *table* to name pictures. We simply made this clear to participants.

Secondly, even if we were to grant that there was a processing cost because of our task instructions, would this not be a good thing? It is a rule of human performance that interference effects are normally stronger, not weaker, in more challenging conditions. Consistent with this, previous research has shown that effects of tDCS are more likely when participants are not performing at ceiling (see Ross et al., 2010; Berryhill, Peterson, Jones & Stephens, 2014). Gauvin et al. failed to mention that we carried out specific analyses to address task difficulty by running separate analyses for responses at different speeds (page 75, section 3.4). Our assumption was that for harder items – indicated by slower naming speeds – we would find a significant effect of tDCS. We still did not find any effect of tDCS.

Thirdly, our longer RTs may reflect the fact that our presentation of the stimuli and trimming procedures allowed longer RTs to be included in our analyses. We displayed pictures for 2500ms or until a response was made. We excluded RTs shorter than 250ms and slower than 2.5 standard deviations from the subject mean, as is standard practice. The other studies cited by Gauvin et al. either presented the picture for a shorter time (e.g., 1500ms in Navarrete et al., 2010 and Belke, 2013) or trimmed longer RTs more (e.g., below 250 and above 2000ms in Howard et al. 2006). Our longer picture display duration alone would have led to longer RTs. We specifically wanted to include longer RTs in order to carry out more detailed analyses according to speed of responses, as mentioned in the paragraph directly above.

2.3.1. Combining Reading and Naming

Gauvin et al. criticized the fact that we asked participants to perform two tasks – reading and picture naming – which ran sequentially. They argued that there could be possible interactions between reading and naming that cancel out any significant effect of tDCS on picture naming. We find this hard to believe. Firstly, there is no reason to assume that reading should interfere with picture naming, given that the same target words were used in the two tasks. When presented first, reading had the purpose of reducing ambiguity of picture names, in line with common practice. Secondly, and crucially, there was no effect of tDCS on reading in any shape or form. It is not clear how Gauvin et al. imagine the null effect in reading would cancel out an otherwise positive effect in naming.

2.4 Data Analysis

Gauvin et al. suggested that the results we obtained with the continuous naming paradigm were different from previously obtained results. This, supposedly, would put into question the validity of all our experiments, and particularly for Experiment 1c, where we targeted the temporal region, which is implicated in lexico-semantic retrieval, and where stimulation produced significant effects in one of the studies by one of the authors of the commentary (Meinzer et al., 2016). Gauvin et al. pointed out that neither ‘lag or session should influence the cumulative interference effect based on previous results (e.g., Belke, 2013)’. Instead, in their reanalysis of data for our control participants – who carried out both sessions without stimulation – Gauvin et al. found an interaction between position, lag and session, which was significant by participants and marginally significant by categories ($F_1(3,78) = 4.07$, $p = .01$,

$\eta^2 = .14$; $F_2(9, 250) = 1.88$, $p = .055$, $\eta^2 = .06$). They claimed that this interaction makes our results uninterpretable, since ‘findings from their Experiment 1b and c with tDCS are confounded by *both* lag and session’. Gauvin et al. then unpacked this three-way interaction by plotting RTs across positions with respect to *lag* separately for the pseudo-sham and the pseudo-real session, and query the fact that plots show a quadratic trend as well as a linear trend, which would be a departure from the original findings by Howard et al. (2006).

Three-way interactions are often difficult to interpret, but they do not preclude interpretation. We have carried out more extensive analyses to address the points raised (for results, see Supplementary Material 1). In 6 out of the 8 analyses, we did not find any three-way interaction of *position*, *lag* and *session*. The only two significant three-way interactions were those found by Gauvin et al. We unpacked them by carrying out separate analyses for each *session* (pseudo-tDCS and pseudo-sham,). For both sessions there was no significant effect of *lag* and no interaction of *lag* by *position*. Instead, an effect of *position* was highly significant or marginally significant in both *sessions* (pseudo-tDCS: $F_1(3, 72) = 6.61$, $p = .001$, $\eta^2 = .22$; $F_2(3, 69) = 3.96$, $p = .012$, $\eta^2 = .15$; pseudo-Sham: $F_1(3, 72) = 2.80$, $p = .046$, $\eta^2 = .10$; $F_2(3, 69) = 2.29$, $p = .09$, $\eta^2 = .09$). Similarly a linear trend across positions was significant in both *sessions* (pseudo-tDCS: $F_1(1, 24) = 9.67$, $p = .01$, $\eta^2 = .29$; $F_2(1, 23) = 5.01$, $p = .04$, $\eta^2 = .18$; pseudo-sham: $F_1(1, 24) = 5.93$, $p = .023$, $\eta^2 = .20$; $F_2(1, 23) = 5.15$, $p = .033$, $\eta^2 = .18$). We do find a significant quadratic trend by participants and marginally by categories for pseudo-tDCS ($F_1(1, 24) = 15.49$, $p = .001$, $\eta^2 = .39$; $F_2(1, 23) = 5.03$, $p = .04$, $\eta^2 = .18$), but not pseudo-sham ($F_1(1, 24) = .34$, $p = .56$, $\eta^2 = .01$; $F_2(1, 23) = .09$, $p = .77$, $\eta^2 = .004$). In Figure 1 (see Supplementary Material 1), we see that interference diminishes with longer lags, particularly at lag 8. This finding is not unique to our data, and was noted recently by Schnur (2014), who reported a reduced interference effect with lags of 8 to 50.

Thus, overall, our results are strongly consistent with the original results by Howard et al. (2006). Three-way interactions are often difficult to interpret especially when they are not in a predicted and/or theoretically meaningful direction. The only two three-way interaction we found are likely to be an uninteresting result which could have happened by chance. There is no indication that the accumulation of interference is systematically influenced by lag and/or session. Gauvin et al. offer no explanation for the three-way interactions and no explanation of how they could have eliminated any significant effect of tDCS, especially since they occurred in a control group that did *not* receive tDCS.

3. Other issues with Gauvin et al

In their conclusion, Gauvin et al. said that we ‘interpret [our] data...as an unsuccessful replication and as evidence that the tDCS technique lacks overall efficiency’, and that this has ‘broader implications for the field. For instance grant reviewers, who are often not expert in the specific field of an application, might be unduly influenced by assertions of ‘failed replications’ and dismiss the importance of continuing the proposed research’.

Gauvin et al.’s conclusion showed a puzzling misinterpretation of our results. We do not interpret our findings as either a direct replication, or as evidence that tDCS ‘...lacks overall efficiency’. We describe our work as failing to find positive effects of tDCS in certain conditions, which we are very careful to specify, and we also outline conditions where tDCS is and/or could be potentially effective, with recommendations for future research. An honest assessment of the tDCS literature shows that *cognitive* effects of tDCS are generally unreliable or weak, especially with healthy participants in single applications, an opinion shared by many researchers (see opinion survey by Riggall et al., 2015). We firmly stand behind our claim that studies have failed to show that tDCS is consistently able to modulate cognition in healthy participants.

Gauvin et al. listed valuable strategies to increase the rigour of the tDCS field, such as direct replication and pre-registration. An important additional strategy, however, is carrying meta-analyses which collate disparate findings and increase power. We have recently carried out such a meta-analysis to assess the foundational claim that tDCS can modify picture naming and word reading (Westwood & Romani, revised manuscript under review). We reviewed 14 papers measuring tDCS effects across a total of 96 conditions. Our intentions were to a) quantify effects of conventional protocols that target language regions (e.g., left hemisphere anodal tDCS administered to temporal/frontal areas), either under normal conditions or conditions that induce semantic interference; b) identify parameters which may moderate the size of the tDCS effect (within conventional stimulation protocols), such as stimulation timing, current density and duration, and atypical protocols (e.g., right hemisphere anodal tDCS or left/right hemisphere cathodal tDCS). In all analyses there was no significant effect of tDCS on overall naming accuracy or speed and no influence on interference effects (these

analyses included the studies mentioned in Table 1 presented in Gauvin et al.). No overall effect of tDCS was found whether or not our studies from Westwood et al. (2017) were included.

Negative results do not mean that research on tDCS should be abandoned, but that efforts should be placed in finding conditions where tDCS is indeed effective. We find it ironic that Gauvin et al. took issue with the justifiably sceptical tone of our paper because it might ‘prevent the field from progressing as funding is diverted elsewhere, and contribute to the perception of experimental psychology as experiencing a replication “crisis”’. Surely unduly inflating the efficacy of tDCS will have an even worse outcome, since time, energy and money will be wasted, and attention diverted from investigating those conditions in which tDCS may in fact be reliable and effective. Such negative repercussions will no doubt damage the reputation of tDCS research (including experimental psychology), and raise important moral and ethical questions, as eloquently delineated by Vincent Walsh, a prominent researcher in the field of non-invasive brain stimulation (Walsh, 2013). Before we conclude, we would like to end our response with a few choice words from Walsh (2013):

‘When my friends and colleagues say that “tDCS is a non-invasive brain stimulation (NIBS) neuromodulatory technique, whose clinical applications to treat pathological neuropsychiatric conditions are rapidly growing [Santarnecchi, Feurra, Galli, Rossi, & Rossi, 2013].” I think they fall into a language trap (in which we all find ourselves) of confusing claims with reality. ... I am all for hope, but when it crosses the line into faith, it becomes an unthinking vehicle. ... [One] consequence of the hype is that the noise may mask important findings. We saw the effects of this with depression and TMS, the advance of which was slowed by premature claims and masked by claims about the utility of TMS in just about every neurological and psychiatric condition. ... We would do better to simply be more honest about the limits of our findings’.

3. Conclusion

We would again like to thank Gauvin et al. for commenting on our work, although we take issue with the fact they repeatedly misrepresented our work. In our response, we have made clear that their criticisms are without merit and they fail to offer adequate alternative explanations for the null effects we report in Westwood et al. (2017). Gauvin et al. (wrongly)

characterized our study as a direct replication and then criticized us for carrying out original experiments rather than trying to exactly replicate previous studies. We see carrying out a fresh series of experiments to assess the ability of tDCS to modulate word production as an important contribution. We find no value in the methodological criticisms raised by Gauvin et al., since our paradigms followed very closely those previously reported in the literature and we obtained very similar behavioural results. This makes us very confident that our paradigms were sensitive to the effects of semantic interference, which we intended to modulate with tDCS.

Finally, we agree that we provided less evidence regarding stimulation of the temporal lobe and more evidence would be desirable. We also agree that if tDCS research is to rise to the rigorous standards that is demanded if potential benefits are to be harvested, then direct replication as well as conceptual replication studies are key. As we said in our conclusion to our paper, one should no longer assume ‘a level of a reliability that is not there’ but rather take the ‘unreliability of tDCS results...as a starting point and as a challenge that needs addressing’.

Our lab is already conducting a direct replication study to assess the effectiveness of tDCS on fluency tasks. Following this commentary, we will also carry out a replication of Meinzer et al. (2016) and Pisoni et al. (2012). These two studies have targeted the left temporal regions, yet both find discrepant results. Clearly differences in protocol may have contributed to differences in outcome, or it may be that tDCS is not reliable. A replication will not only contribute to the exchange above, but also to the debate about whether tDCS can in fact modulate word production and, especially, semantic interference effects.

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